the treatment of other diseases where mediators are known or can be identified. The practical implications of this research are far reaching, including the development of high potency compounds which might be beneficial to alkali-injured eyes or other types of diseases.

The *in vitro* experiments have conclusively shown that the (D) and (L) RTR tetramer was highly inhibitory to the neutrophil chemoattractants released in the early stages in the alkali-injured eye. When this tetramer was applied to the alkali-injured rabbit eye a statistically significant decrease in corneal ulceration was identified when compared to the control group. The affinity of the RTR tetramer for the chemoattractants appearing after alkali-injury defeat their polymorphonuclear leukocyte chemotactic properties immediately and thereby reduce ulceration in the short and long term. Proof for this latter statement is found in the continuing protective effect past day 33 when all medication had been stopped.

N-acetyl-PGP and N-methyl-PGP are the primary neutrophil chemoattractants released into the stroma by direct hydrolysis of corneal proteins immediately after an alkali-injury. These chemoattractants are thought to trigger the subsequent heavy

infiltration of neutrophils that leads to corneal ulceration. It is likely that the complementary binding of RTR tetramer to N-acetyl-PGP and N-methyl-PGP, shortly after the injury, inactivated these chemoattractants in the cornea, reducing the early and then subsequent neutrophilic invasion. Exclusion of polymorphonuclear leukocytes protects the injured corneal tissue from the degradative enzymes and oxygen free radicals contained in these inflammatory cells. These considerations explain the persistent therapeutic effect of RTR treatment and suggest that early treatment of the alkali-injured eye, for a shorter interval, might yield a similar result.

This experiment demonstrates that (D) and (L)-RTR tetramer, used alternately in the same eye, significantly reduced the incidence of corneal ulcers occurring after alkali-injury. The potential for enzymatic degradation of peptides at different stages of healing in an alkali-injured cornea is unknown. A paucity of corneal cells in the first few days after the injury would be consistent with low enzymatic activity in this time period. Other studies report that (D)-antisense peptides have similar biologic activity to (L)-peptides and that (D)-peptides are stable <u>in vivo</u>.[18,19,29] Corneal enzymes might be capable of degrading the (L)-RTR tetramer. The rationale

for administering both tetramers on alternate hours to the same eye was to prevent enzymatic degradation of a portion of the tetramer, keeping the total RTR tetramer concentration higher

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